

**REMARKS**

Favorable reconsideration, reexamination, and allowance of the present patent application are respectfully requested in view of the foregoing amendments and the following remarks. No new matter has been added by the foregoing amendments, and full support for such amendments can be found in the original claims, and in the specification at page 33, line 27 to page 34, line 6.

***Information Disclosure Statement***

Applicants note that the office action from the Chinese Patent Office listed on the PTO-1449 submitted with the Information Disclosure Statement filed on April 6, 2004 has not been considered by the Examiner. The Examiner alleges that the office action is listed as a foreign patent document, but alleges that it is not a foreign patent document. The M.P.E.P. only requires that a 'listing' of material information be provided; the use of the PTO-1449 is not even required. Therefore, applicants assert that the office action from the Chinese Patent Office has been properly cited. However, a new PTO-1449 has been submitted herewith, listing the office action as an "other" document. Consideration is respectfully requested.

***Objection to the Claims***

At page 3 of the Office Action, Claim 17 was objected to because it allegedly recites an improper alternative expression. Claim 17 has been amended to address this issue and Applicant respectfully requests reconsideration of this objection.

For at least the foregoing reasons, Applicant respectfully submits that Claim 17 is not objectionable, and therefore respectfully requests withdrawal of the objection thereto.

***Rejection under 35 U.S.C. § 112, second paragraph***

In the Office Action, beginning at page 3, Claims 1-2, 5, 7-10, 12-13, and 26-31

were rejected under 35 U.S.C. § 112, second paragraph, as reciting subject matters that allegedly are unclear for the recitation of “hybridizes”. Applicant respectfully requests reconsideration of this rejection.

In paragraph 10, the Office Action alleges that the claims are unclear in the recitation of “hybridizes”. Although applicant respectfully disagrees with the Examiner’s assertion, the claims have been amended to remove this language. Although applicants assert that the claims were clear, they have been amended in the interests of advancing prosecution, and therefore, it is respectfully requested that this rejection be withdrawn.

For at least the foregoing reasons, Applicant respectfully submits that Claims 1-2, 5, 7-10, 12-13, and 26-31 fully comply with 35 U.S.C. § 112, second paragraph, and therefore respectfully requests withdrawal of the rejection thereof under 35 U.S.C. § 112.

***Rejection under 35 U.S.C. § 112, first paragraph***

In the Office Action, beginning at page 4, Claims 1-2, 5, 7-10, 12-13, 16-17, 20-21 and 26-31 were rejected under 35 U.S.C. § 112, first paragraph, as reciting subject matters that allegedly contain subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Applicant respectfully requests reconsideration of this rejection.

Applicants respectfully disagree with the above assertions and allegations, and respectfully assert that claimed invention is fully and adequately described by the specification. It is respectfully asserted that the full scope of the claims is clearly described so that a person ordinarily skilled in the art could make and use the invention commensurate in scope with these claims. The claims have been amended to remove the hybridization language, and instead the bacterial strain and the proteins contained within are described by their structural characteristics.

The Examiner’s arguments focus on the undue experimentation required to

determine all *Methylophilus* bacteria having enhanced activity of dihydrodipicolinate synthase and/or aspartokinase. The genes and proteins having enhanced activity are not novel sequences, but are known in the art. The prior art must be considered when determining undue experimentation and undue breadth of claims, and there is a body of literature of the genes/proteins, their sequences, and their activities in various strains of bacteria. We previously submitted data which shows an alignment comparing amino acid sequences of dihydrodipicolinate synthase and aspartokinase of *M. methylotropus* with those of other microorganisms. These alignments show conserved regions and non-conserved regions, which would clearly allow someone of skill in the art to fully determine other species within the genus that would function as described and claimed. Furthermore, two literature references are provided as appendix B (Zhang et al. and Parkhill et al.), which show sequences and analysis thereof of aspartokinase from *Amycolatopsis mediterranei* and dihydrodipicolinate synthase from *Neisseria meningitides*, respectively. One of ordinary skill, armed with this knowledge in the art of the claimed genes/proteins from other species, the exemplified mutations of the genes and proteins, and the high level of skill in this art, would clearly be able to determine other species that when transformed into the particular claimed strain of *Methylophilus* would have the activity of producing L-amino acids. The methods for determining L-amino acid production are well-known and routine to the skilled art worker.

On page 7, the Office Action alleges that the “genus encompasses species that are widely variant with respect to: 1) the method of enhancing dihydrodipicolinate synthase activity and/or enhanced aspartokinase activity.” Applicants submit that the methods for achieving enhancement of the recited enzymes are clearly described by the specification. A method of enhancing dihydrodipicolinate synthase and/or aspartokinase activity is described by ligating a gene fragment coding for these enzymes with a vector that functions in the chosen host, and transforming the vector into the host. This method results in increasing the copy number of the genes (see page 13, line 25 to page 18, line

12).

Another method for enhancing the enzymes' activities is described beginning on page 18, line 13, which describes procedures for placing multiple copies of the genes encoding these enzymes into the chromosome of the chosen host by performing homologous recombination or using a transposon. This method also increases the copy number of these genes in the host organism, resulting in enhanced activity of the enzymes.

Yet a third method is described beginning on page 19, line 3, which describes amplifying the activities by replacing an expression control sequence such as a promoter with a known stronger promoter. All of the well-described methods in the specification are further depicted in the prior art (see references cited in the noted portions of the specification), and therefore, when the teachings and descriptions of the specification are combined with the knowledge in the art concerning such methods, the methods are clearly and adequately described.

For at least the foregoing reasons, Applicant respectfully submits that Claims 1-2, 5, 7-10, 12-13, 16-17, 20-21 and 26-31 fully comply with 35 U.S.C. § 112, first paragraph, and therefore respectfully requests withdrawal of the rejection thereof under 35 U.S.C. § 112.

In the Office Action, beginning at page 8, Claims 1-2, 5, 7-10, 12-13, 16-17, 20-21, and 26-31 were rejected under 35 U.S.C. § 112, 1<sup>st</sup> paragraph as allegedly not being enabled by the specification. Applicants assert that it would not require undue experimentation for the skilled art worker to determine other species which fall within the genus of dihydrodipicolinate synthase and aspartokinase genes/proteins, since many sequences from other microorganisms are known in the art. Based on the alignment submitted with our previous response, one of ordinary skill could easily determine regions of the genes/proteins tolerant to change and those not tolerant to change, thereby

easily determining other members of the genus. Such determinations would not require undue experimentation since there is much knowledge in the art concerning these sequences, and the skill level in this art is very high.

Furthermore, one of ordinary skill in the art could easily determine methods for enhancing the activities of the enzymes depicted in the claims without undue experimentation, particularly since at least 3 such methods are clearly and completely described in the specification. As described above, at least 3 methods are described in the specification, and such general methods are also well known in the art. For at least the foregoing reasons and for those outlined above, Applicant respectfully submits that Claims 1-2, 5, 7-10, 12-13, 16-17, 20-21 and 26-31 fully comply with 35 U.S.C. § 112, first paragraph, and therefore respectfully requests withdrawal of the rejection thereof under 35 U.S.C. § 112.

***Rejection under 35 U.S.C. § 102***

In the Office Action, beginning at page 10, Claims 16-17 and 20-21 were rejected under 35 U.S.C. § 102, as reciting subject matters that allegedly are anticipated by Kojima et al. (WO 95/16042). Applicant respectfully requests reconsideration of this rejection.

Applicant respectfully disagrees with the Examiner's assertion and interpretation of the word "several". Nevertheless, applicants have amended the claims to recite that only 1-10 amino acids can be substituted, deleted, added, or inverted in the amino acid sequences of the claimed enzymes. Applicants assert that the amino acid sequences of AK and DDPS disclosed in WO95/16042 are different from SEQ ID NO: 6 or SEQ ID NO: 10 of the present invention in clearly more than 10 amino acids. As such, it is believed that the isolated DNA of claims 16-17 and 20-21 is not anticipated by WO95/16042.

For at least the foregoing reasons, Applicant respectfully submits that the subject

matters of Claims 16-17 and 20-21 are not anticipated by Kojima et al., are therefore not unpatentable under 35 U.S.C. § 102, and therefore respectfully requests withdrawal of the rejection thereof under 35 U.S.C. § 102.

***Conclusion***

For at least the foregoing reasons, Applicant respectfully submits that the present patent application is in condition for allowance. An early indication of the allowability of the present patent application is therefore respectfully solicited.

If Examiner Steadman believes that a telephone conference with the undersigned would expedite passage of the present patent application to issue, he is invited to call on the number below.

It is not believed that extensions of time are required, beyond those that may otherwise be provided for in accompanying documents. However, if additional extensions of time are necessary to prevent abandonment of this application, then such extensions of time are hereby petitioned under 37 C.F.R. § 1.136(a), and the undersigned respectfully requests that she be contacted immediately.

Respectfully submitted,

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